## *Clinical manifestations of MPS VI*

| *Organ system* | *Complications* |
|---|---|
| ***Ear, nose, throat, and respiratory*** [1,2] | GAG accumulation in the oropharynx and airway, combined with typical dysmorphic features and restrictive lung disease, can cause<br>• Thickening of the nose, lips, and tongue<br>• Severe hearing impairment<br>• Recurrent otitis media<br>• Narrow trachea and excessive and thickened secretions<br>• Obstructive sleep apnea<br>• Recurrent pulmonary infections and pneumonia<br>• Skeletal problems and reduced lung function and volume<br>• The need for a respiratory device such as a CPAP machine or surgical insertion of an endotracheal tube to aid breathing |
| ***Cardiovascular*** [3-5] | Cardiovascular abnormalities are a major cause of morbidity and mortality among patients with MPS VI<br>• Heart murmurs<br>• Mitral and aortic valve degeneration<br>• Electrocardiographic abnormalities<br>• Coronary artery disease<br>• Systemic vascular narrowing and hypertension<br>• Cardiomyopathy |
| ***Skeletal*** [2-4] | Skeletal deformities and other clinical manifestations are seen in patients with MPS VI<br>• Dysostosis multiplex<br>• Spinal cord or nerve root injury<br>• Coarse facial features<br>• Short stature<br>• Joint abnormalities<br>• Chest rib cage restriction<br>• Growth impairment<br>• Profound dwarfism<br>• Limited mobility<br>• Claw hands |
| ***Ophthalmic*** [3, 4, 6, 7] | Visual impairment occurs in ~40% of patients with MPS VI<br>• Most patients are farsighted<br>• Corneal clouding occurs in 95% of all patients<br>• Retinopathy<br>• Optic nerve abnormalities<br>• Ocular hypertension and glaucoma |
| ***Dental*** [8] | Dental abnormalities are common in patients with MPS VI and include<br>• Mandibular condylar hypoplasia<br>• Malposition of unerupted teeth<br>• Large dental follicles<br>• Anterior open bite<br>• Maxillary constriction<br>• Taurodontism |
| ***CNS/PNS*** [3,4] | MPS VI involves no direct impairment of CNS activity, such that the patient's intelligence is typically normal despite the great physical disease burden<br>• GAG accumulation causes carpal tunnel syndrome, intracranial pressure, and progressive compressive myelopathy<br>• Loss of dexterity and fixed flexion<br>• CNS stenosis and spinal cord compression<br>• Severe pain caused by compressed or traumatized nerves and nerve roots |
| ***Organ systems*** [3] | The abdomen in patients with MPS VI is large and protruding due to the enlarged liver and spleen, often with the presence of inguinal and/or umbilical hernia |

Abbreviations: CNS, central nervous system; CPAP, continuous positive airway pressure; GAG, glycosamnoglycan; MPS VI, mucopolysaccharidosis VI; PNS, peripheral nervous system.

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